

This listing of the claims will replace all prior versions, and listings, of claims in the application:

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1. (original) A pharmaceutical composition comprising, in combination with an effective amount of a bioactive agent, a targeted matrix which comprises a polymer and a targeting ligand, wherein said targeting ligand is covalently associated with said polymer and said bioactive agent is associated non-covalently with said polymer, and wherein said bioactive agent is substantially homogeneously dispersed throughout said matrix.

2. (original) A pharmaceutical composition according to Claim 1 wherein said polymer comprises repeating alkylene groups, wherein each alkylene group optionally contains from one to three heteroatoms selected from -O-, -N(R)- or -S(O)_n-, where R is hydrogen or alkyl and n is 0 to about 1000.

3. (original) A pharmaceutical composition according to Claim 2 wherein said polymer is selected from the group consisting of a polyalkylene oxide, polyalkyleneimine, polyalkylene amine, polyalkene sulfide, polyalkylene sulfonate, polyalkylene sulfone, poly(alkylenesulfonylalkyleneimine) and copolymers thereof.

4. (original) A pharmaceutical composition according to Claim 3 wherein said polymer is selected from the group consisting of a polyethylene glycol, polypropylene glycol, branched polyethylene imine, polyvinyl pyrrolidone, polylactide, poly(lactide-co-glycolide), polysorbate, polyethylene oxide, poly(ethylene oxide-co-propylene oxide), poly(oxyethylated) glycerol, poly(oxyethylated) sorbitol, poly(oxyethylated glucose), polymethyloxazoline, polyethyloxazoline, polyhydroxyethyloxazoline, polyhydroxypropyloxazoline, polyvinyl alcohol, poly(hydroxyalkylcarboxylic acid), polyhydroxyethyl acrylic acid, polyhydroxypropyl methacrylic acid, polyhydroxyvalerate, polyhydroxybutyrate, polyoxazolidine, polyaspartamide, polysialic acid, linear polypropylene imine, polyethylene sulfide, polypropylene sulfide, polyethylenesulfonate, polypropylenesulfonate, polyethylene sulfone, polyethylenesulfonylethyleneimine, polycaprolactone, polypropylene oxide, polyvinylmethylether, polyhydroxyethyl acrylate, polyhydroxypropyl methacrylate, polyphosphazene and derivatives, mixtures and copolymers thereof.

5. (original) A pharmaceutical composition according to Claim 4 wherein said polymer is selected from the group consisting of a polyethylene glycol and polypropylene glycol and copolymers thereof.

6. (original) A pharmaceutical composition according to Claim 5 wherein said polymer is polyethylene glycol.

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7. (original) A pharmaceutical composition according to Claim 1 wherein said polymer comprises a polypeptide.

8. (original) A pharmaceutical composition according to Claim 1 wherein said bioactive agent is an anti-cancer agent.

9. (original) A pharmaceutical composition according to Claim 8 wherein said anti-cancer agent is selected from the group consisting of paclitaxel, docetaxel, camptothecin, and derivatives and analogs thereof.

10. (original) A pharmaceutical composition according to Claim 9 wherein said anti-cancer agent is paclitaxel.

11. (original) A pharmaceutical composition according to Claim 9 wherein said anti-cancer agent is docetaxel.

12. (original) A pharmaceutical composition according to Claim 9 wherein said anti-cancer agent is camptothecin.

13. (original) A pharmaceutical composition according to Claim 1 wherein said bioactive agent has limited water solubility.

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14. (original) A pharmaceutical composition according to Claim 13 wherein the ratio of the solubility of said bioactive agent in said polymer to the solubility of said bioactive

agent in water is greater than about 1:1.

15. (original) A pharmaceutical composition according to Claim 14 wherein said ratio is at least about 10:1.

16. (original) A pharmaceutical composition according to Claim 1 wherein said targeting ligand targets cells or receptors associated with diseased tissue.
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17. (original) A pharmaceutical composition according to Claim 1 wherein said targeting ligand is selected from the group consisting of proteins, peptides, cytokines, growth factors, vitamins, vitamin analogues, polysaccharides, glycopeptides, glycoproteins, steroids, steroid analogs, hormones, cofactors, bioactive agents, genetic material, drug molecules, and antagonists of the GPIIIBIIIA receptor of platelets.

18. (original) A pharmaceutical composition according to Claim 17 wherein said targeting ligand is selected from the group consisting of proteins and peptides.

19. (original) A pharmaceutical composition according to Claim 18 wherein said targeting ligand comprises a peptide.

20. (original) A pharmaceutical composition according to Claim 19 wherein said peptide is selected from the group consisting of linear peptides and cyclized peptides.

21. (original) A pharmaceutical composition according to Claim 19 wherein said peptide targets cells or receptors associated with tissue selected from the group consisting of brain, kidney, lung, skin, pancreas, intestine, uterus, adrenal gland and retina tissue.

22. (original) A pharmaceutical composition according to Claim 21 wherein said peptide targets cells or receptors associated with brain tissue.

23. (currently amended) A pharmaceutical composition according to Claim 22 wherein said peptide comprises a sequence selected from the group consisting of

CNSRLHLRC (SEQ ID NO: 3), CENWWGDVC (SEQ ID NO: 4),
WRCVLREGPAGGCAWFNRHRL (SEQ ID NO: 5), and CLSSRLDAC (SEQ ID NO: 6).

24. (original) A pharmaceutical composition according to Claim 21 wherein said peptide targets cells or receptors associated with kidney tissue.

25. (currently amended) A pharmaceutical composition according to Claim 24 wherein said peptide comprises a sequence selected from the group consisting of CLPVASC (SEQ ID NO: 7) and CGAREMC (SEQ ID NO: 8).

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26. (original) A pharmaceutical composition according to Claim 21 wherein said peptide targets cells or receptors associated with lung tissue.

27. (currently amended) A pharmaceutical composition according to Claim 26 wherein said peptide comprises a sequence selected from the group consisting of CGFECVRQCPERC (SEQ ID NO: 33), CGFELETG (SEQ ID NO: 34), CTLRDRNC (SEQ ID NO: 35) and CIGEVEVC (SEQ ID NO: 36).

28. (original) A pharmaceutical composition according to Claim 21 wherein said peptide targets cells or receptors associated with skin tissue.

29. (currently amended) A pharmaceutical composition according to Claim 28 wherein said peptide comprises the sequence CVALCREACGEGC (SEQ ID NO: 37).

30. (original) A pharmaceutical composition according to Claim 21 wherein said peptide targets cells or receptors associated with pancreas tissue.

31. (currently amended) A pharmaceutical composition according to Claim 30 wherein said peptide comprises the sequence SWCEPGWCR (SEQ ID NO: 38).

32. (original) A pharmaceutical composition according to Claim 21 wherein said peptide targets cells or receptors associated with intestinal tissue.

33. (currently amended) A pharmaceutical composition according to Claim 32 wherein said peptide comprises the sequence YSGKKGW (SEQ ID NO: 39).

34. (original) A pharmaceutical composition according to Claim 21 wherein said peptide targets cells or receptors associated with uterine tissue.

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35. (currently amended) A pharmaceutical composition according to Claim 34 wherein said peptide comprises the sequence GLSGGGRS (SEQ ID NO: 40).

36. (original) A pharmaceutical composition according to Claim 21 wherein said peptide targets cells or receptors associated with adrenal gland tissue.

37. (currently amended) A pharmaceutical composition according to Claim 36 wherein said peptide comprises the sequence LMLPRAD (SEQ ID NO: 41).

38. (original) A pharmaceutical composition according to Claim 21 wherein said peptide targets cells or receptors associated with retinal tissue.

39. (currently amended) A pharmaceutical composition according to Claim 38 wherein said peptide comprises a sequence selected from the group consisting of CRDVVSVIC (SEQ ID NO: 42) and CSCFRDVCC (SEQ ID NO: 43).

40. (original) A pharmaceutical composition according to Claim 19 wherein said peptide inhibits integrin-expressing cells from binding to extracellular matrix proteins.

41. (original) A pharmaceutical composition according to Claim 40 wherein said peptide inhibits the binding of fibronectin to $\alpha 5-\beta 1$ integrin.

42. (currently amended) A pharmaceutical composition according to Claim 41 wherein said peptide comprises a sequence selected from the group consisting of CRGDC (SEQ ID NO: 9), CRGDCL (SEQ ID NO: 10), NGR(AHA) (SEQ ID NO: 11), DGR(AHA) (SEQ

ID NO: 12), CRGDCA (SEQ ID NO: 13), RCDVVV (SEQ ID NO: 14), SLIDIP (SEQ ID NO: 15), TIRSVD (SEQ ID NO: 16), KRGD (SEQ ID NO: 17), RRGPD (SEQ ID NO: 18) and RGDL (SEQ ID NO: 19).

43. (original) A pharmaceutical composition according to Claim 19 wherein said peptide forms RGD-type binding determinants of antibodies.

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44. (currently amended) A pharmaceutical composition according to Claim 43 wherein said peptide is selected from the group consisting of CSFGRGDIRNC (SEQ ID NO: 20), CSFGRTDQRIC (SEQ ID NO: 21), CSFGKGDNRIC (SEQ ID NO: 22), CSFGRNDSRNC (SEQ ID NO: 23), CSFGRVDDRNC (SEQ ID NO: 24), CSFGRADRRNC (SEQ ID NO: 25), CSFGRSVDRNC (SEQ ID NO: 26), CSFGKRDMRNC (SEQ ID NO: 27), CSFGRWDARNC (SEQ ID NO: 28), CSFGRQDVRCN (SEQ ID NO: 29) and CSFGRDDGRNC (SEQ ID NO: 30).

45. (original) A pharmaceutical composition according to Claim 19 wherein said peptide targets angiogenic endothelium associated with solid tumors.

46. (currently amended) A pharmaceutical composition according to Claim 45 wherein said peptide comprises a sequence selected from the group consisting of CDCRGDCFC (SEQ ID NO: 31) and CNGRCVSGCAGRC (SEQ ID NO: 32).

47. (original) A pharmaceutical composition according to Claim 19 wherein said peptide targets receptors associated with cancer cells.

48. (original) A pharmaceutical composition according to Claim 47 wherein said peptide is selected from the group consisting of Abaecins, Andropins, Apidaecins, AS, Bactenecins, Bac, Bactericidins, Bacteriocins, Bombinins, Bomblotins, BPTI, Brevinins, Cecropins, Charybdotoxins, Coleoptericins, Crabolinins, α -Defensins, β -Defensins, Defensins-insect, Defensins-scorpion, Dermaseptins, Dipteridins, Drosocins, Esculentins, Indolicidins, Lactoferricins, Lantibiotics, Leukocons, Magainins, Mastoparans, Melittins, Phormicins, Polypheusins, Protegrins, Royalisins, Sarcotoxins, Seminal Plasmins, Tachypleins, Thionins and Toxins.

49. (original) A targeted matrix for use as a delivery vehicle for a bioactive agent, wherein the matrix comprises a polymer that is covalently associated with a targeting ligand.

50. (original) A targeted matrix according to Claim 49 which has a morphology selected from the group consisting of particulate and micellar.

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51. (original) A targeted matrix according to Claim 50 which has a particulate morphology.

52. (original) A targeted matrix according to Claim 51 wherein said particles have a diameter of from about 1 nm to about 1000 nm.

53. (original) A targeted matrix according to Claim 52 wherein said particles have a diameter of from about 10 nm to about 500 nm.

54. (original) A targeted matrix according to Claim 53 wherein said particles have a diameter of from about 20 nm to about 200 nm.

55. (original) A targeted matrix according to Claim 49 wherein said polymer comprises repeating alkylene groups, wherein each alkylene group optionally contains from one to three heteroatoms selected from -O-, -N(R)- or -S(O)_n-, where R is hydrogen or alkyl and n is 0 to about 1000.

56. (original) A targeted matrix according to Claim 55 wherein said polymer is selected from the group consisting of a polyalkylene oxide, polyalkyleneimine, polyalkylene amine, polyalkene sulfide, polyalkylene sulfonate, polyalkylene sulfone, poly(alkylenesulfonylalkyleneimine) and copolymers thereof.

57. (original) A pharmaceutical composition according to Claim 56 wherein said polymer is selected from the group consisting of a polyethylene glycol, polypropylene

glycol, branched polyethylene imine, polyvinyl pyrrolidone, polylactide, poly(lactide-co-glycolide), polysorbate, polyethylene oxide, poly(ethylene oxide-co-propylene oxide), poly(oxyethylated) glycerol, poly(oxyethylated) sorbitol, poly(oxyethylated glucose), polymethyloxazoline, polyethyloxazoline, polyhydroxyethyloxazoline, polyhydroxypropyloxazoline, polyvinyl alcohol, poly(hydroxyalkylcarboxylic acid), polyhydroxyethyl acrylic acid, polyhydroxypropyl methacrylic acid, polyhydroxyvalerate, polyhydroxybutyrate, polyoxazolidine, polyaspartamide, polysialic acid, linear polypropylene imine, polyethylene sulfide, polypropylene sulfide, polyethylenesulfonate, polypropylenesulfonate, polyethylene sulfone, polyethylenesulfonylethyleneimine, polycaprolactone, polypropylene oxide, polyvinylmethylether, polyhydroxyethyl acrylate, polyhydroxypropyl methacrylate, polyphosphazene and derivatives, mixtures and copolymers thereof.

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58. (original) A targeted matrix according to Claim 57 wherein said polymer is selected from the group consisting of a polyethylene glycol and polypropylene glycol and copolymers thereof.

59. (original) A targeted matrix according to Claim 49 wherein said polymer is selected from the group consisting of linear, branched and star structures.

60. (original) A targeted matrix according to Claim 59 wherein said polymer is a branched structure.

61. (original) A targeted matrix according to Claim 60 wherein said branched structure comprises from about 4 to about 10 arms.

62. (original) A targeted matrix according to Claim 61 wherein said branched structure comprises from about 4 to about 8 arms.

63. (original) A targeted matrix according to Claim 59 wherein said polymer has a star structure.

64. (original) A targeted matrix according to Claim 63 wherein said star structure comprises from about 3 to about 12 arms.

65. (original) A targeted matrix according to Claim 64 wherein said star structure comprises from about 4 to about 8 arms.⁷

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66. (original) A targeted matrix according to Claim 49 wherein said polymer comprises a polypeptide.

67. (original) A targeted matrix according to Claim 49 wherein said targeting ligand is selected from the group consisting of proteins, peptides, cytokines, growth factors, vitamins, vitamin analogues, polysaccharides, glycopeptides, glycoproteins, steroids, steroid analogs, hormones, cofactors, bioactive agents, genetic material, drug molecules, and antagonists of the GPIIBIIIA receptor of platelets.

68. (original) A targeted matrix according to Claim 67 wherein said targeting ligand is selected from the group consisting of proteins and peptides.

69. (original) A targeted matrix according to Claim 68 wherein said targeting ligand comprises a peptide.

70. (original) A targeted matrix according to Claim 69 wherein said peptide is selected from the group consisting of linear peptides and cyclized peptides.

71. (original) A targeted matrix according to Claim 69 wherein said peptide targets cells or receptors associated with tissue selected from the group consisting of brain, kidney, lung, skin, pancreas, intestine, uterus, adrenal gland and retina tissue.

72. (original) A targeted matrix according to Claim 71 wherein said peptide targets cells or receptors associated with brain tissue.

73. (currently amended) A targeted matrix according to Claim 72 wherein said

peptide comprises a sequence selected from the group consisting of CNSRLHLRC (SEQ ID NO: 3), CENWWGDVC (SEQ ID NO: 4), WRCVLREGPAGGCAWFNRHRL (SEQ ID NO: 5), and CLSSRLDAC (SEQ ID NO: 6).

74. (original) A targeted matrix according to Claim 71 wherein said peptide targets cells or receptors associated with kidney tissue.

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75. (currently amended) A targeted matrix according to Claim 74 wherein said peptide comprises a sequence selected from the group consisting of CLPVASC (SEQ ID NO: 7) and CGAREMC (SEQ ID NO: 8).

76. (original) A targeted matrix according to Claim 71 wherein said peptide targets cells or receptors associated with lung tissue.

77. (currently amended) A targeted matrix according to Claim 76 wherein said peptide comprises a sequence selected from the group consisting of CGFECVRQCPERC (SEQ ID NO: 33), CGFELETC (SEQ ID NO: 34), CTLRDRNC (SEQ ID NO: 35) and CIGEVEVC (SEQ ID NO: 36).

78. (original) A targeted matrix according to Claim 71 wherein said peptide targets cells or receptors associated with skin tissue.

79. (currently amended) A targeted matrix according to Claim 78 wherein said peptide comprises the sequence CVALCREACGEGC (SEQ ID NO: 37).

80. (original) A targeted matrix according to Claim 71 wherein said peptide targets cells or receptors associated with pancreas tissue.

81. (currently amended) A targeted matrix according to Claim 80 wherein said peptide comprises the sequence SWCEPGWCR (SEQ ID NO: 38).

82. (original) A targeted matrix according to Claim 71 wherein said peptide targets

cells or receptors associated with intestinal tissue.

83. (currently amended) A targeted matrix according to Claim 82 wherein said peptide comprises the sequence YSGKKGW (SEQ ID NO: 39).

84. (original) A targeted matrix according to Claim 71 wherein said peptide targets cells or receptors associated with uterine tissue.
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85. (currently amended) A targeted matrix according to Claim 84 wherein said peptide comprises the sequence GLSGGRS (SEQ ID NO: 40).

86. (original) A targeted matrix according to Claim 71 wherein said peptide targets cells or receptors associated with adrenal gland tissue.

87. (currently amended) A targeted matrix according to Claim 86 wherein said peptide comprises the sequence LMLPRAD (SEQ ID NO: 41).

88. (original) A targeted matrix according to Claim 71 wherein said peptide targets cells or receptors associated with retinal tissue.

89. (currently amended) A targeted matrix according to Claim 88 wherein said peptide comprises a sequence selected from the group consisting of CRDVVSVIC (SEQ ID NO: 42) and CSCFRDVCC (SEQ ID NO: 43).

90. (original) A targeted matrix according to Claim 71 wherein said peptide inhibits integrin-expressing cells from binding to extracellular matrix proteins.

91. (original) A targeted matrix according to Claim 90 wherein said peptide inhibits the binding of fibronectin to $\alpha 5-\beta 1$ integrin.

92. (currently amended) A targeted matrix according to Claim 91 wherein said peptide is selected from the group consisting of CRGDC (SEQ ID NO: 9), CRGDCL (SEQ ID

NO: 10), NGR(AHA) (SEQ ID NO: 11), DGR(AHA) (SEQ ID NO: 12), CRGDCA (SEQ ID NO: 13), RCDVVV (SEQ ID NO: 14), SLIDIP (SEQ ID NO: 15), TIRSVD (SEQ ID NO: 16), KRGD (SEQ ID NO: 17), RRGPD (SEQ ID NO: 18) and RGDL (SEQ ID NO: 19).

93. (original) A targeted matrix according to Claim 69 wherein said peptide forms RGD-type binding determinants of antibodies.

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94. (currently amended) A targeted matrix according to Claim 93 wherein said peptide is selected from the group consisting of CSFGRGDIRNC (SEQ ID NO: 20), CSFGRTDQRIC (SEQ ID NO: 21), CSFGKGDNRIC (SEQ ID NO: 22), CSFGRNDSRNC (SEQ ID NO: 23), CSFGRVDDRNC (SEQ ID NO: 24), CSFGRADRRNC (SEQ ID NO: 25), CSFGRSVDRNC (SEQ ID NO: 26), CSFGKRDWRNC (SEQ ID NO: 27), CSFGRWDARNC (SEQ ID NO: 28), CSFGRQDVRNC (SEQ ID NO: 29) and CSFGRDDGRNC (SEQ ID NO: 30).

95. (original) A targeted matrix according to Claim 49 wherein said peptide targets angiogenic endothelium associated with solid tumors.

96. (currently amended) A targeted matrix according to Claim 95 wherein said peptide comprises a sequence selected from the group consisting of CDCRGDCFC (SEQ ID NO: 31) and CNGRCVSGCAGRC (SEQ ID NO: 32).

97. (original) A targeted matrix according to Claim 49 wherein said peptide targets receptors associated with cancer cells.

98. (original) A targeted matrix according to Claim 97 wherein said peptide is selected from the group consisting of Abaecins, Andropins, Apidaecins, AS, Bactenecins, Bac, Bactericidins, Bacteriocins, Bombinins, Bompolitins, BPTI, Brevinins, Cecropins, Charybdotoxins, Coleoptericins, Crabolinins, α -Defensins, β -Defensins, Defensins-insect, Defensins-scorpion, Dermaseptins, Dipterincins, Drosocins, Esculentins, Indolicidins, Lactoferricins, Lantibiotics, Leukocons, Magainins, Mastoparans, Melittins, Phormicins, Polypheusins, Protegrins, Royalisins, Sarcotoxins, Seminal Plasmins, Tachypleins, Thionins and Toxins.

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Appl'd

99. (original) A method for enhancing the bioavailability of a bioactive agent *in vivo* comprising (i) providing a pharmaceutical composition which comprises, in combination with an effective amount of a bioactive agent, a matrix comprising a polymer and a targeting ligand, and (ii) administering to a patient said pharmaceutical composition, wherein said targeting ligand is associated covalently with said polymer and said bioactive agent is associated non-covalently with said polymer, and wherein said bioactive agent is substantially homogeneously dispersed throughout said matrix.

100. (original) A method for treating cancer comprising administering to a patient a pharmaceutical composition comprising, in combination with an effective amount of an anticancer agent, a matrix which comprises a polymer and a targeting ligand, wherein said targeting ligand is covalently associated with said polymer and said anticancer agent is associated non-covalently with said polymer, and wherein said anticancer agent is substantially homogeneously dispersed throughout said matrix.
